THE AMENDMENTS

In the Specification

Amend the title at page 1, lines 1-2, to:

~~NOVEL~~ METHODS OF DIAGNOSING BREAST CANCER~~, COMPOSITIONS, AND METHODS OF SCREENING FOR BREAST CANCER MODULATORS~~

At page 1, line 3, before "FIELD OF THE INVENTION," insert the following paragraph:

This application is a CIP of 09/525,361, filed March 15, 2000; which is a CIP of 09/453,137, filed December 2, 1999; which is a CIP of 09/450,810, filed November 29, 1999, abandoned; and a CIP of 09/268,865, filed March 15, 1999.

Amend the paragraph starting at page 14, line 10 to:

Another example of a useful algorithm is the BLAST algorithm, described in Altschul et al., J. Mol. Biol. 215, 403-410, (1990) and Karlin et al., PNAS USA 90:5873-5787 (1993). A particularly useful BLAST program is the WU-BLAST-2 program which was obtained from Altschul et al., Methods in Enzymology, 266: 460-480 (1996) ~~[http://blast.wustl/edu/blast/ READ.html]~~. WU-BLAST-2 uses several search parameters, most of which are set to the default values. The adjustable parameters are set with the following values: overlap span =1, overlap fraction = 0.125, word threshold (T) = 11. The HSP S and HSP S2 parameters are dynamic values and are established by the program itself depending upon the composition of the particular sequence and composition of the particular database against which the sequence of interest is being searched; however, the values may be adjusted to increase sensitivity. A % amino acid sequence identity value is determined by the number of matching identical residues divided by the total number of residues of the "longer" sequence in the aligned region. The "longer" sequence is the one having the most actual residues in the aligned region (gaps introduced by WU-Blast-2 to maximize the alignment score are ignored).

Amend the paragraph starting at page 10, line 13 to:

In a preferred embodiment, breast cancer sequences are those that are up-regulated in breast cancer; that is, the expression of these genes is higher in breast carcinoma as compared to normal breast tissue. "Up-regulation" as used herein means at least about a 50% increase, preferably a two- fold change, more preferably at least about a three fold change, with at least about five-fold

or higher being preferred. All accession numbers herein are for the GenBank sequence database and the sequences of the accession numbers are hereby expressly incorporated by reference. GenBank is known in the art, see, e.g., Benson, DA, et al., Nucleic Acids Research 26:1-7 (1998) ~~and http://www.ncbi.nlm.nih.gov/~~. In addition, these genes were found to be expressed in a limited amount or not at all in bone marrow, heart, brain, lung, liver, kidney, muscle, pancreas, prostate, colon, skin, testes, stomach, small intestine and spleen.

Amend the paragraph starting at page 18, line 20:

Alternatively, the oligonucleotides may be synthesized on the surface, as is known in the art. For example, photoactivation techniques utilizing photopolymerization compounds and techniques are used. In a preferred embodiment, the nucleic acids can be synthesized *in situ*, using well known photolithographic techniques, such as those described in WO 95/25116; WO 95/35505; U.S. Patent Nos. 5,700,637 and 5,445,934; and references cited within, all of which are expressly incorporated by reference; these methods of attachment form the basis of the Affimetrix ~~GeneChip™~~ GENECHIP® (DNA microarray chip) technology.

Amend the paragraph starting at page 33, line 4:

"Differential expression," or grammatical equivalents as used herein, refers to both qualitative as well as quantitative differences in the genes' temporal and/or cellular expression patterns within and among the cells. Thus, a breast cancer gene can qualitatively have its expression altered, including an activation or inactivation, in, for example, normal versus breast cancer tissue. That is, genes may be turned on or turned off in a particular state, relative to another state. As is apparent to the skilled artisan, any comparison of two or more states can be made. Such a qualitatively regulated gene will exhibit an expression pattern within a state or cell type which is detectable by standard techniques in one such state or cell type, but is not detectable in both. Alternatively, the determination is quantitative in that expression is increased or decreased; that is, the expression of the gene is either upregulated, resulting in an increased amount of transcript, or downregulated, resulting in a decreased amount of transcript. The degree to which expression differs need only be large enough to quantify via standard characterization techniques as outlined below, such as by use of Affymetrix ~~GeneChip™~~ GENECHIP® (DNA microarray chip) expression arrays, Lockhart, Nature Biotechnology, 14:1675-1680 (1996), hereby expressly incorporated by reference. Other techniques include, but are not limited to, quantitative reverse transcriptase PCR, Northern analysis and RNase protection. As outlined above, preferably the change in expression (i.e. upregulation or downregulation) is at least about 50%, more preferably

at least about 100%, more preferably at least about 150%, more preferably, at least about 200%, with from 300 to at least 1000% being especially preferred.

Amend the paragraph starting at page 44, line 4:

Generally, in a preferred embodiment of the methods herein, the breast cancer protein or the candidate agent is non-diffusably bound to an insoluble support having isolated sample receiving areas (e.g. a microtiter plate, an array, etc.). It is understood that alternatively, soluble assays known in the art may be performed. The insoluble supports may be made of any composition to which the compositions can be bound, is readily separated from soluble material, and is otherwise compatible with the overall method of screening. The surface of such supports may be solid or porous and of any convenient shape. Examples of suitable insoluble supports include microtiter plates, arrays, membranes and beads. These are typically made of glass, plastic (e.g., polystyrene), polysaccharides, nylon or nitrocellulose, ~~teflon™~~ TEFLON® (synthetic resinous flurorine-containing polymers), etc. Microtiter plates and arrays are especially convenient because a large number of assays can be carried out simultaneously, using small amounts of reagents and samples. The particular manner of binding of the composition is not crucial so long as it is compatible with the reagents and overall methods of the invention, maintains the activity of the composition and is nondiffusable. Preferred methods of binding include the use of antibodies (which do not sterically block either the ligand binding site or activation sequence when the protein is bound to the support), direct binding to "sticky" or ionic supports, chemical crosslinking, the synthesis of the protein or agent on the surface, etc. Following binding of the protein or agent, excess unbound material is removed by washing. The sample receiving areas may then be blocked through incubation with bovine serum albumin (BSA), casein or other innocuous protein or other moiety.

Amend the paragraph starting at page 55, line 5:

Purification of poly A^+ mRNA from total RNA. Heat oligotex suspension to 37°C and mix immediately before adding to RNA. Incubate Elution Buffer at 70°C. Warm up 2 x Binding Buffer at 65°C if there is precipitate in the buffer. Mix total RNA with DEPC-treated water, 2 x Binding Buffer, and ~~Oligotex~~ OLIGOTEX® (chemicals for the purification of nucleic acids) according to Table 2 on page 16 of the ~~Oligotex~~ OLIGOTEX® Handbook. Incubate for 3 minutes at 65°C. Incubate for 10 minutes at room temperature.

Amend the paragraph starting at page 55, line 10:

Centrifuge for 2 minutes at 14,000 to 18,000 g. If centrifuge has a "soft setting," then use it. Remove supernatant without disturbing ~~Oligotex~~ OLIGOTEX® (chemicals for the purification of nucleic acids) pellet. A little bit of solution can be left behind to reduce the loss of ~~Oligotex~~ OLIGOTEX®. Save sup until certain that satisfactory binding and elution of poly A^+ mRNA has occurred.

Amend the paragraph starting at page 56, line 3:

Clean up total RNA using Qiagen's ~~Rneasy~~ RNEASY® (chromatographic materials for separation of nucleic acids) kit

Add no more than 100ug to an ~~Rneasy~~ RNEASY® column. Adjust sample to a volume of 100ul with RNase- free water. Add 350ul Buffer RLT then 250ul ethanol (100%) to the sample. Mix by pipetting (do not centrifuge) then apply sample to an ~~Rneasy~~ RNEASY® mini spin column. Centrifuge for 15 sec at >10,000rpm. If concerned about yield, re-apply flowthrough to column and centrifuge again.

Amend the paragraph starting at page 57, line 23:

~~Rneasy~~ RNEASY® clean-up of IVT product

Follow previous instructions for ~~Rneasy~~ RNEASY® columns or refer to Qiagen's ~~Rneasy~~ RNEASY® protocol handbook.